

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
18 December 2003 (18.12.2003)

PCT

(10) International Publication Number
WO 2003/104432 A3

(51) International Patent Classification⁷: **C07K 16/00**,
A61K 39/395, C07H 21/04

(21) International Application Number:
PCT/US2003/018373

(22) International Filing Date: 9 June 2003 (09.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/387,293 7 June 2002 (07.06.2002) US
60/411,032 16 September 2002 (16.09.2002) US

(71) Applicant (for all designated States except US): **THE GOVERNMENT OF THE UNITED STATES, AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3084 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **PASTAN, Ira, H.** [US/US]; 11710 Beall Mountain Road, Potomac, MD 20854 (US). **NAGATA, Satoshi** [JP/US]; 6070 California Circle 413, Rockville, MD 20852 (US). **ONDA, Masanori** [JP/US]; 320 Lorraine Drive, Rockville, MD 20852 (US). **NUMATA, Yoshito** [JP/JP]; 2-451-1-311 Hirano Kashiwara, Osaka, Osaka 581-0019 (JP). **SANTORA, Kenneth** [US/US]; 10543 Wheatley Street, Kensington, MD 20895 (US). **BEERS, Richard** [US/US]; 5306 Russett Road, Rockville, MD 20853 (US). **KREITMAN, Robert** [US/US]; 11915 Reynolds Avenue, Potomac, MD 20854 (US). **SINHA, Abhishek** [US/US]; 11533 Aliento Court, San Diego, CA 92127 (US).

(74) Agents: **HYMAN, Laurence, J. et al.**; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW. ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- of inventorship (Rule 4.17(iv)) for US only

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
16 September 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **ANTI-CD30 STALK AND ANTI-CD30 ANTIBODIES SUITABLE FOR USE IN IMMUNOTOXINS**

(57) Abstract: CD30 is a receptor expressed on cells of Hodgkin's disease and certain leukemias. The extracellular portion of CD30 is cleaved, releasing a form known as sCD30. The invention relates in part to the discovery that a residual, extracellular "stalk" of CD30 remains after cleavage of sCD30. The stalk provides an advantageous and previously unrecognized target for immunotoxins. The invention provides antibodies that bind to the CD30 stalk or to epitopes destroyed upon the cleavage of CD30 which results in the stalk. The invention further provides new anti-CD30 antibodies that form effective immunotoxins and are particularly suitable for making disulfide stabilized Fv ("dsFv")-immunoconjugates. The dsFv immunoconjugates can be used as reagents to label CD30-expressing cancer cells or to inhibit the growth of CD30-expressing cancer cells. Moreover, the invention provides anti-CD30 antibodies that activate complement-dependent cytotoxicity.



WO 2003/104432 A3

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US03/18373

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 16/00; A61K39/395; C07H21/04

US CL : 530/387.1, 387.3, 388.23, 391.1;424/130.1, 133.1, 143.1, 178.1, 183.1;536/23.53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/387.1, 387.3, 388.23, 391.1;424/130.1, 133.1, 143.1, 178.1, 183.1;536/23.53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	U.S. 6,033,876 (LEMKE et al) 3 March 2000 (03.03.2000), see entire document.	38-45, 52-69, 71-72, 75-82.

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

27 April 2004 (27.04.2004)

Date of mailing of the international search report

04 AUG 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

David J Blanchard

Telephone No. (703) 308-1123

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 373

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claim Nos.: 21-26, 46-51, 70, 73 and 74
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 21-26, 46-51, 70, 73 and 74 are non-statutory "use" claims. The claims recite a use without any active, positive steps delimiting how this use is actually practiced.
2. ☒ Claim Nos.: 1-20 and 27-37
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Please See Continuation Sheet
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

Continuation of Box I Reason 2:

Claims 1-20 and 27-37 are drawn to antibody compositions and nucleic acids encoding antibodies that bind to SEQ ID NO:1 (CD30 stalk), however SEQ ID NO:1 is not provided in the sequence listing and a search of terms such as "CD30" and "stalk" and "antibody" would not be meaningful.

Continuation of B. FIELDS SEARCHED Item 3:

WEST, Medline, Biosis, EMBASE, Biotechno, Geneseq, Issued and Published patents, Swissprot, PIR 78, SPTREMBL.

Search terms: SEQ ID Nos.2, 4, 6, 7, 11-15, 17, 21-22, 26-29, 38-41, CD30, antibody, antibody T24, T420, T427, T405, T408, inventor search.